REMARKS

Reconsideration of this application, as amended, is respectfully requested. The Applicants wish to draw the Examiner's attention to the applicants' related co-pending applications and issued patents (see Appendix A) directed to nanoparticles and methods of preparation and use thereof.

The Applicants note that the Examiner did not return an executed PTO 1449 form for the 6th Supp. IDS that was hand-delivered to the Examiner on September 9, 2002. Subsequent to the issuance of this Office action, the Applicants had filed a 7th Supp. IDS. The Applicants request that the Examiner fully execute the PTO 1449 forms for the 6th and 7th Supp. IDS and return a copy of the executed PTO 1449 forms to the undersigned representative. Copies of the initial IDS, 6th and 7th Supplemental IDS, and associated PTO 1449 forms are attached. The Examiner is requested to contact the undersigned representative if the Examiner would like to have another copy of the references.

The specification has been amended to update the priority claim. No new matter has been added to the application as a result of this amendment.

Claims 1-22 and 433-444 were originally pending in this application. Claims 1-22 and 435-444 were amended to further clarify the invention or to correct the form. The amended claims are fully supported in the previously pending claims and the specification, and thus do not constitute new matter. The amended claims are supported, for example, by the original claims and the specification in Example 5 (page 90); Example 7 (page 95); and Example 19 (page 131, line 37 to page 136, line 16). Accordingly, no new matter has been introduced into the application as a result of the above amendment. Claims 1-22 and 433-444 remain pending in this application.

Turning to the office action, claim 1 stands rejected under 35 U.S.C. section 102(b) as bein anticipated by Giles et al. (WO 92/04469)("Giles"). Claims 1, 2, 4, 6, and 11-20 also stand rejected under 35 U.S.C. section 102(b) as being anticipated by Olson (WO 90/02205) ("Olson"). Finally, claims 1, 2, 4-8, 11-17, and 19-21 stand rejected under 35 U.S.C. section 102(e) as being anticipated by Yguerabide et al. U.S. Patent No. 6,214,560 ("Yguerabide"). The Applicants respectfully traverse these rejections.

As a general rule, for prior art to anticipate under section 102, every element of the claimed invention must be identically disclosed in a single reference. Corning Glass Works v. Sumitomo Electric, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious, from a reference is enough to negate anticipation. Connell v. Sears, Roebuck & Co., 220 U.S.P.Q 193, 1098 (Fed. Cir. 1983). Applicants respectfully submit that neither Giles, Olson or Yguerabide can be applied to support the anticipation rejections of the claims.

Specifically, the Examiner alleged that Giles described methods for detecting the presence of nucleic acid sequences by agglutination using a generic particle reagent. Giles' discussion of the particle agglutination method is found on pages 3 and 6. The particle reagent is further described on pages 7 to 8. The Examiner also alleged that Olson described methods for detecting the presence of nucleic acid sequences by agglutination using two or more non-complementary probes. Olson's agglutination method is described in the bottom of page 7 to the top of page 13. A discussion of Olson's probes begins on page 14. The Examiner further alleged that Yguerabide taught detection and measurement of one or more analytes in a sample using particles of specific composition and size using light scattering. The discussion is found starting in col. 82, line 35, of Yguerabide. Col. 83 provides further discussion regarding the particle binding to a surface. There is no discussion or suggestion of any nanoparticle-oligonucleotide probes for detecting a nucleic acid target or any method of use thereof wherein the complexes formed between the nanoparticle probes and the nucleic acid targets have a "sharp melting profile and an increased melting temperature" relative to a melting profile and a melting temperature of analogous complexes formed with the nucleic acid and an unlabeled or fluorophore-labeled oligonucleotides to "allow for selective discrimination of any nucleotide insertion, deletion, or mismatch in the nucleic acid" See present claims 1 and 2. None of the cited references suggest anywhere a method that employs nanoparticle probes that produce complexes with nucleic acid targets that have sharp melting profiles, increased melting temperatures, and extraordinary discrimination properties associated therewith.

The presently claimed methods that employ nanoparticle-labeled probes that form complexes with target nucleic acids having sharp melting profiles and increased melting temperatures relative to analogous complexes formed with unlabeled or fluorophore labeled

probes provide certain advantages which are both surprising and unexpected since the aforementioned recited properties allow for extraordinary discrimination between perfectly matched and mismatched nucleic acid targets relative to complexes including unlabeled or fluorophore-labeled oligonucleotides. For instance, as shown in Figure 12 and discussed in Example 5 (page 90 in the specification), nanoparticle labeled oligonucleotide probes were prepared and contacted with various target nucleic acids under stringent conditions. With fully matched targets, the complex produced a positive result (blue color); with targets having one mismatched base, no complex formation occurred with the probes. In Figure 35(b), dehybridization of nanoparticle – labeled targets from capture strands bound to a surface was much more sensitive to temperature than that of an analogous fluorophore-labeled targets with identical sequences (Figure 35(a)). In addition, Figure 36 shows images of model oligonucleotide arrays challenged with unlabeled synthetic target and fluorescent-labeled (Figure 36(a)) or nanoparticle-labeled (Figure 36(b)) probes. That Figure showed that arrays challenged with model target and nanoparticle labeled probes and stained with silver solution clearly exhibited highly selective hybridization to complementary array elements and that the selectivity of the nanoparticle-based arrays was higher than that of the fluorophore-indicated arrays. See also the specification at page 135, lines 12-28. Thus, the Applicant respectfully submits that neither Giles or Olson can be applied to support anticipation rejections of the claims under section 102(b). Furthermore, the Applicant respectfully submits that Yguerabide cannot be applied to support an anticipation rejection of the claims under section 102(e). Withdrawal of the rejections is in order and is respectfully requested.

In conclusion, the Applicants respectfully submit that the claims in this application are in allowable condition and request a Notice to this effect.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned

representative if the Examiner believes that this would be helpful in expediting the prosecution of this application.

Respectfully submitted,

Dated: Oct. 10, 2003

Emily Miao
Reg. No. 35,285

McDonnell Boehnen
Hulbert & Berghoff, Ltd.
300 South Wacker Drive
Chicago, IL 60606
Telephone: 312-913-0001
Facsimile: 312-913-0001

APPENDIX A

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
00-653-A	U.S. 09/927,777 Filed 8/10/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garamella, Li, Park/ NANOPARTICLES HAVING OLIGONUCLEOTIDES ATTACHED THERETO AND USES THEREFORE	PENDING
00-713-B1	09/923,625 Filed 8/7/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTIDES ATTACHED THERETO AND USES THEREFOR	PENDING
00-713-C	09/344,667, filed 6/25/99	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTIDES ATTACHED THERETO AND USES THEREFORE	U.S. Patent No. 6,361,944, issued 3/26/02
00-713-I	U.S.S.N 09/603,830 Filed 6/26/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; NANOPARTICLES HAVING OLIGONUCLEOTIDES ATTACHED THERETO AND USES THEREFOR	U.S. Patent No. 6,506,564, issued 1/14/03
00-713-I-1	09/961,949 9/20/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton;	U.S. Patent No. 6,582,921, issued June 24, 2003

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		NANOPARTICLES HAVING OLIGONUCLEOTIDES ATTACHED THERETO AND USES THEREFOR	
00-713-I-2	09/957,318 9/20/01	See 00-713-I-1	PENDING
00-713-I-3	09/957,313 9/20/01	See 00-713-I-1	ALLOWED
00-713-I-4	09/966,491 9/28/01	See 00-713-I-1	U.S. Patent No. 6,610,491
00-713-I-5	09/966,312 9/28/01	See 00-713-I-1	ALLOWED
00-713-I-6	09/967,409 9/28/01	See 00-713-I-1	PENDING
00-713-I-7	09/974,500 10/10/01	See 00-713-I-1	ALLOWED
00-713-I-8	09/974,007 10/10/01	See 00-713-I-1	PENDING
00-713-I-9	09/973,638 10/10/01	See 00-713-I-1	PENDING
00-713-I-10	09/973,788 10/10/01	See 00-713-I-1	ALLOWED
00-713-I-11	09/975,062 10/11/01	See 00-713-I-1	ALLOWED
00-713-I-12	09/975,376 10/11/01	See 00-713-I-1	PENDING
00-713-I-13	09/975,384 10/11/01	See 00-713-I-1	PENDING
00-713-I-14	09/975,498 10/11/01	See 00-713-I-1	ALLOWED

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
00-713-I-15	09/975,059 11/11/01	See 00-713-I-1	PENDING
00-713-I-16	09/976,601 10/12/01	See 00-713-I-1	PENDING
00-713-I-17	09/976,968 10/12/01	See 00-713-I-1	PENDING
00-713-I-18	09/976,971 10/12/01	See 00-713-I-1	ALLOWED
00-713-I-19	09/976,863 10/12/01	See 00-713-I-1	PENDING
00-713-I-20	09/976,577 10/12/01	See 00-713-I-1	ALLOWED
00-713-I-21	09/976,618 10/12/01	See 00-713-I-1	PENDING
00-713-I-22	09/981,344 10/15/01	See 00-713-I-1	PENDING
00-713-I-23	09/976,900 10/12/01	See 00-713-I-1	PENDING
00-713-I-24	09/976,617 10/12/01	See 00-713-I-1	PENDING
00-713-I-25	09/976,378 10/12/01	See 00-713-I-1	PENDING
00-713-i-26	10/410,324 04/10/03	See 00-713-I-1	PENDING
00-713-L	U.S.S.N. 09/693,005 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTIDES ATTACHED THERETO AND	U.S. Patent No. 6,495,324, issued 12/17/02

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		USES THEREFORE	
00-713-M	U.S.S.N. 09/693,352 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTIDES ATTACHED THERETO AND USES THEREFORE	U.S. Patent No. 6,417,340, issued 7/9/02
00-714-G	U.S. 09/830,620 Filed 8/15/01	Mirkin, Nguyen/ NANOPARTICLES WITH POLYMER SHELLS	PENDING
00-715-A	U.S. 09/760,500 Filed 1/12/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; Garamella, Li/ METHOD OF ATTACHING OLIGONUCLEOTIDES TO NANOPARTICLES AND PRODUCTS PRODUCED THEREBY	ALLOWED
00-1085-A	U.S.S.N. 09/820,279 Filed 3/28/01	Mirkin,Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS	ALLOWED
00-1086-A	U.S. 09/903,461 Filed 7/11/01	Letsinger, Garimella/ METHOD OF DETECTION BY ENHANCEMENT OF SILVER STAINING	U.S. Patent No. 6,602,669, Filed 8/5/03
01-565-A	USSN 10/125,194 Filed 4/18/02	Mirkin, Nguygen, Watson, Park/ OLIGONUCLEOTIDE-MODIFIED ROMP POLYMERS AND CO-	PENDING

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		POLYMERS	
01-599-A	U.S.S.N. 10/291,291 Filed 11/08/02	Storhoff/NOVEL THIOL-BASED METHOD FOR ATTACHING OLIGONUCLEOTIDES TO NANOPARTICLES	PENDING
01-661-A	U.S.S.N. 10/034,451 Filed 12/28/01	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-661-C	U.S.S.N. 10/153,483 Filed 5/22/02	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-661-E	U.S.S.N. 10/397,579 3/26/03	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-1565-A	U.S.S.N. 10/266,983 Filed 10/08/02	Park, Taton, Mirkin/ARRAY-BASED ELECTRICAL DETECTION OF DNA USING NANOPARTICLE PROBES	PENDING
01-1705-A	U.S.S.N. 10/108,211 Filed 3/27/02	Nam, Park, Mirkin/BIO-BARCODES BASED ON OLIGONUCLEOTIDE-MODIFIED NANOPARTICLES	PENDING
02-338-B	USSN 10/172,428 Filed 6/14/02	Cao, Jin, Nam, Mirkin/MULTICHANNEL DETECTION USING NANOPARTICLE PROBES WITH	PENDING

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		RAMAN SPECTROSCOPIC FINGERPRINTS	
02-338-C	10/431,341 5/7/03	Cao, Jin, Nam, Mirkin/MULTICHANNEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	PENDING